UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 23 1990

Memorandum:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#9F3763. DPX-V9360 (Nicosulfuron, ACCENT™) in/on corn. Evaluation of Analytical Method and Residue Data. (DEB#'s 5324, 5325, 5326, 6408, and 6409; MRID#'s 409242-01, -02, -03, and -04, 409545-01, 410826-01, -26, -27, -28, -29, -30, -31, -32, and -33).

FROM: Jerry B. Stokes, Chemist
Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Richard D. Schmitt, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

EXPEDITE

TO: Robert Taylor, PM-25
Fungicide-Herbicide Branch
Registration Division (H7505C)

and

Toxicology Branch
Health Effects Division (H7509C)

E.I. DuPont de Nemours and Company, Inc., Agriculture Products Department has requested the establishment of tolerances for residues of DPX-V9360 [nicosulfuron, Accent™, 3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl)aminocarbonyl)aminosulfonyl)) -N,N-dimethyl] for the proposed herbicide use in/on raw agricultural commodities of corn grain (0.1 ppm), corn forage (0.1 ppm), corn fodder (0.1 ppm), and corn silage (0.1 ppm). No tolerances are proposed for milk, meat, fat, or meat by-products (including liver and kidney) of cattle, goats, hogs, horses, and sheep or, the meat, fat, and meat by-products (including liver and kidney) of poultry, or eggs, or no food/feed additive tolerances are proposed in accordance with 40 CFR 180.6(b).

This is a new chemical and no temporary or permanant tolerances are currently established or pending on any raw agricultural commodity, or in livestock meat, fat, meat byproducts (including liver and kidney), milk, or eggs, or for any processed commodities.

DEB recently recommended in favor of Section 18 exemptions requested by Tennessee Dept. of Agriculture to control johnsongrass in field corn. DEB determined that based upon the proposed postemergence use DPX-V9360 residues would not exceed 0.1 ppm

for corn forage, silage, fodder, or grain. No secondary residues of DPX-V9360 were expected in milk, meat, fat, meat byproducts (including liver and kidney) of cattle, horses, swine, sheep, goats, or meat, fat, meat byproducts (including liver and kidney), or eggs of poultry. Also no residues of DPX-V9360 were expected in processed food or feed items for this Section 18. (See memo of 1/25/90, A. Aikens).

Summary of Conclusions:

1. The petitioner must submit the following:

   a. CAS#'s for some impurities in the TGAI,

   b. Analysis of one additional production batch,

   c. Clarification of solvent solubilities for DPX-V9360,

   d. Revised CSF for ACCENT™ Technical (352-LGL).

2. EFGWB (EFED) should be made aware of rotational crop restrictions.

3a. The nature of the residue is adequately understood for the corn plant.

3b. The soil pH's used in the metabolism study and in the 8X application for the processing study must be submitted.

3c. The nature of the residue is adequately understood in ruminants.

3d. A poultry metabolism study may be needed.

4a. Adequate analytical methodology must be submitted for corn fodder for DPX-V9360 residues.

4b. Analytical enforcement methodology may be needed for metabolite pyridine sulfonamide in all corn r.a.c's.

4c. Analytical enforcement methodology may be needed for DPX-V9360 and/or metabolite pyridine sulfonamide residues in livestock meat and/or milk and/or eggs.

4d. Confirmational data are needed for HPLC analytical enforcement methodology.

4e. The Zorbax™Rx column must be adequately defined.

4f. FDA multiresidue protocol IV tested for parent; others are not applicable for parent; Testing of protocols may be needed for pyridine sulfonamide.

5a. The residue data and storage stability data adequately support the proposed 0.1 ppm tolerances.

5b. However, additional residue data are required to determine if the requested DPX-V9360 tolerances can be decreased to 0.05 ppm.

5c. Residue data and storage stability data are requested for metabolite pyridine sulfonamide for the all corn r.a.c.'s and processed commodities of oil and meal.

5d. A ruminant and/or poultry feeding study may be needed.

5e. Tolerances may be needed for meat/milk/poultry/eggs for DPX-V9360 and/or metabolite pyridine sulfonamide.

5f. Feed/food additive tolerances may be needed.

6. There are no Codex, or Canadian or Mexican limits; therefore, there are no problems of incompatibility.

Conclusions

1a. Petitioner must provide the Chemical Abstracts chemical reference nos. (CAS#'s), if and/or when available, for all impurities listed in the TGAI.

1b. Petitioner must report data for one more batch of TGAI. Only the analyses for 4 batches are reported.

1c. Solubilities are listed for DPX-V9360 in benzene and tetrahydrofuran as 2.7 and 2.6, respectively, in MRID#409545-01, but as 1.7 and 26, respectively, in MRID#409242-03. The petitioner must clarify the correct solubilities.

1d. Petitioner must submit a revised CSF for ACCENT™ Technical (352-LGL). The certified limit of one impurity is stated incorrectly. (See Confidential Appendix for more details.)

2. Rotational crop restrictions are dependent upon the US location and the soil pH: winter cereals, 3-15 months; field corn, anytime; soybeans, 8 months; spring cereals, 8-18 months; alfalfa, 9-15 months; clover, 9-15 months; dry beans, 8-20 months, and sorghum, 9-20 months. Alfalfa, clover, dry beans, and sorghum require a field assay in selected states if the soil pH >7.0. For other crops not listed a field bioassay is recommended before planting. Rotational crop restrictions listed above may not be acceptable according to the Agency policy (See memo of 1/14/87 E. Tinsworth, RD) in regards to rotational crops after application of a pesticide. The Environmental Fate and Ground Water Branch in EFED should be made aware of these restrictions.

3a. The nature of the residue in the corn plant is adequately understood for the proposed use, i.e., the primary residue of regulatory concern is the parent, DPX-V9360. The need to include metabolite pyridine sulfonamide will be determined after the requested residue data (See conclusion 5b) have been reviewed.

3b. The pH of the soil used in the plant metabolism study must be submitted.

3c. The nature of the residue in the ruminants is adequately understood for the proposed use, i.e., the residue of regulatory concern is the parent, DPX-V9360.

3d. The nature of the residue in poultry may not be adequately understood. The need for a poultry metabolism study will be determined after the requested residue data (See conclusion 5b) have been reviewed.

4a. An analytical enforcement method has been submitted for the parent only. The methodology is adequate for enforcement purposes for the residues of DPX-V9360 in corn forage and grain. Before we determine the adequacy of the proposed enforcement method on corn fodder, the petitioner should submit the characteristics of the corn fodder supplied to the Agency laboratory for the PMV, e.g., maturity at harvest, moisture content, with or without ears, etc. After reviewing this information the proposed enforcement method may require rewriting or modification for this commodity. The petitioner should also specify in the clarification/rewrite of the method that the pH levels of all mobile phases must be closely monitored and maintained accurately according to instructions. The petitioner must properly define the Zorbax™Rx column. Is it a C8 or C18 bonded phase? No methods were submitted for any plant metabolites. If pyridine sulfonamide is added to the tolerance expression, then enforcement methodology and a method validation by the Agency laboratory will be needed.

4b. Additional data, i.e., sample HPLC charts to adequately support the procedure outlined (i.e., pH alteration of HPLC solvent) for the analysis for DPX-V9360 residues in the presence of other interferring pesticides, should be submitted to DEB for review.

4c. Analytical enforcement methods may be needed for cattle, horses, swine, and sheep meat, fat, and meat byproducts (including liver and kidney). The requested residue data (See conclusion 5b) must be reviewed before this need can be determined.

4d. Analytical enforcement methods may be needed for poultry meat, fat, and meat byproducts (including liver and kidney). The requested additional residue data (See conclusion 5b) must be reviewed before this need can be determined.

4e. DPX-V9360 was analyzed by the FDA Protocol IV. The parent did not give a detectable response on the HPLC/ fluorescence detector system. No metabolites were analyzed. Protocols I, II, or III were not run because DPX-V9360 is thermally labile and not suitable for GLC analysis. If metabolite pyridine sulfonamide is added to the tolerance expression, then this residue must be evaluated with the FDA multiresidue protocols.

5a. The residue data adequately support the proposed 0.1 ppm tolerances for DPX-V9360 in/on corn forage, corn fodder, corn silage, and corn grain. However, based upon the submitted residue data these tolerances could possibly be decreased to 0.05 ppm. Before making a final conclusion on the appropriate tolerance levels in corn, additional residue data are required for parent DPX-V9360 in all corn r.a.c.'s from the states listed in the Group B and C on the proposed label. Also another PMV may have to be performed if our final recommendation is the 0.05 ppm level for the parent DPX-V9360.

5b. Residue data are also required for the metabolite pyridine sulfonamide from six different US locations (3 samples of forage, 3 samples of fodder, and 3 samples of grain from each location) using samples which have already been analyzed for parent DPX-V9360. Appropriate storage stability data are also needed for the pyridine sulfonamide. The need for tolerances for metabolite pyridine sulfonamide will be determined after review of the requested field residue data.

5c. DEB must first review the additional residue data (See conclusion 5b) before a determination can be made with respect to 40 CFR 180.6(a) for the secondary residues in meat, milk, poultry, and eggs.

5d. The need for tolerances for meat, fat, meat byproducts (including liver and kidney), or eggs of poultry can not be determined until the additional residue data (See conclusion 5b) have been reviewed.

5e. No ruminant feeding studies were submitted. The goat metabolism study adequately represented an exaggerated feeding level. DEB, at this time, will not require a ruminant feeding study. However, when real residues of DPX-V9360 occur in livestock feed items, a ruminant feeding study may be required. Also, if the metabolite pyridine sulfonamide is determined to be of regulatory concern, then a ruminant feeding study may be needed.

5f. A poultry feeding study may be required, and is dependent upon the results of the requested additional residue data (See conclusion 5b).

5g. Food/feed additive tolerances may not be needed. No detectable DPX-V9360 residues (<0.05 ppm) were found in corn grain treated at 8.0 oz a.i./A (8X of label rate) or in the resulting processed commodities, corn oil or corn meal, from such grain. Storage stability data are adequate for the proposed herbicide use on field corn. However, these samples (grain, meal, and oil) must be analyzed for metabolite pyridine sulfonamide. Storage stability data should be included for this metabolite. The petitioner must also submit the pH of the soil used in the 8X application rate.

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5h. Storage stability data for the parent DPX-V9360 are adequate for the proposed herbicide use on field corn.

6. No Codex tolerances, or Canadian, or Mexican Limits are established for a food use for DPX-V9360. Therefore, there are no problems of incompatabilty.

Recommendations

DEB recommends against the establishment of tolerances for DPX-V9360 (nicosulfuron) for the proposed postemergence use on field corn until deficiencies 1a, 1b, 1c, 1d, 3a, 3b, 3d, 4a, 4b, 4c, 4d, 4e, 5a, 5b, 5c, 5d, 5e, 5f, and 5g have been satisfied.

EFGWB should be made aware of the rotational crop restrictions as noted in conclusion 2.

PRODUCT CHEMISTRY

INTRODUCTION

The Product Chemistry Data Requirements as given in 40 CFR 158.150, 158.160, 158.162, 158.167, 158.170, 158.175, 158.180, and 158.190 are listed below along with the appropriate Product Chemistry Guideline references, and the submitted product chemistry data. Corresponding to each of the Topical Discussions listed below is the Guidelines Reference No. in "Data Requirements for Pesticide Registration; Final Rule" of May 4, 1988 (53 FR 15952), which explains the minimum data the Agency will need to adequately assess the product chemistry of DPX-V9360 (nicosulfuron, ACCENT™).

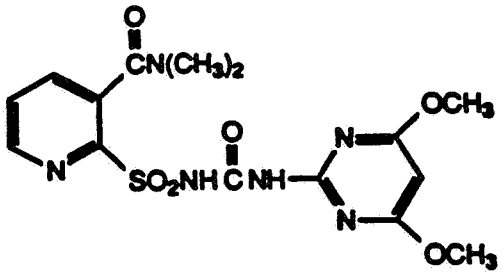
	Guidelines Reference No.	40 CFR No.
Product Identity and Composition	61-1	158.150
	61-2	158.160, 158.162
	61-3	158.167
Analysis and Certification of Product Ingredients	62-1	158.170
	62-2	158.175
	62-3	158.180
Physical and Chemical Characteristics	63-(2-13)	158.190

Product Chemistry Data Requirements
Guideline reference:

61-1: Product Identity and Disclosure of Ingredients (40 CFR 158.155)

The registrant is required to provide the name, nominal concentration, and certified limits of each active ingredient and the name, nominal concentration, and upper limit of each impurity. For each active ingredient the information should include the molecular, empirical, or structural formulas; the CA name, the CAS number; and the molecular weight.

The structure of the active ingredient (DPX-V93602) in ACCENT™ is the following:



The chemical name for the active ingredient in ACCENT™ is 3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl) aminocarbonyl)aminosulfonyl))-N,N-dimethyl. The common name is nicosulfuron (ISO approved, ANSI proposed). Other identifying characteristics and codes are:

Empirical Formula: $C_{15}H_{18}N_6O_6S$
Molecular Weight: 410.40
CAS Registry No: 111991-09-4

DEB Comments/Conclusions

No additional information is required for the structure, CA name, CAS number, or molecular weight. Information was obtained from MRID#409242-01. Nominal concentrations and certified limits are discussed in the Confidential Appendix under 62-1 and 62-2.

61-2: Description of the Beginning Materials and Manufacturing Process (40 CFR 158.160, 158.162); Description of the Formulation Process (40 CFR 158.165)

The guidelines require that the suppliers of beginning materials be identified and that full descriptions of the beginning materials be provided. The description of the manufacturing process should include a discussion of each individual reaction in the process, the relative amounts of the reacting materials, the physical conditions of each step, and any purification procedures.

The guidelines also require a description of the formulation process of the proposed product, pertaining to the characterizations of the process, the ingredients in the process, the process equipment, and the incorporated quality control measures.

The registrant has submitted data in response to these requirements; these data are given and discussed in the Confidential Appendix.

DEB Comment/Conclusions

The beginning materials are adequately discussed and sufficient data have been submitted for the manufacturing process.

No additional data are needed.

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The petitioner has submitted adequate data in regards to the identification of the ingredients and subsequent technical specifications for the proposed formulation, ACCENT™.

No additional information is required for the formulation process.

61-3: Discussion of formation of impurities (40 CFR 158.167)

The petitioner must discuss the potential or actual impurities in the product, and why they may be present, based upon established chemical theory and on what the petitioner knows about the composition of beginning materials, the inerts, and the TGAI (and any contamination or degradation of the TGAI), and desired and side reactions of the production or formulation process.

The petitioner has submitted a discussion of the possible impurities in the proposed product. Details are listed in the Confidential Appendix.

DEB Comments/Conclusions

Adequate data have been submitted in regards to the formation of possible impurities in the production of DPX-V9360. (MRID#409545-01). No additional data are needed.

62-1: Preliminary analysis (40 CFR 158.170)
62-2: Certification of limits (40 CFR 158.175)

Five or more samples, representative of different manufactured batches, should be analyzed by appropriate methods for active ingredients and each impurity with results given for well-known, accepted procedures or a complete description should be given including validation of precision and accuracy.

A certification of upper and lower limits of the active ingredients and upper limits of each impurity is required for the technical material. A certification of the upper and lower limits of the active ingredient and each intentionally added inert is also required for the formulation. The values for the limits should be based upon a consideration of the values for the actual levels of samples. An discussion of the procedures used to establish the certified limits is required. [Dietary Exposure Branch (DEB) defines the technical grade of the active ingredient (TGAI) as the active ingredient plus the impurities associated with the chemical synthesis.].

The data that the registrant has submitted in response to these requirements are discussed in the Confidential Appendix.

DEB Comments/Conclusions

Analyses data have been submitted for 4 production lots of DPX-V9360 (MRID#409545-01). A Confidential Statement of Formula for the

certification of limits for the TGAI has been submitted. Both the data and the CSF are discussed in the Confidential Appendix.

- Petitioner must provide the Chemical Abstracts chemical reference nos. (CAS#'s), if and/or when available, for all impurities listed in the TAGI.

- Petitioner must report data for one more batch of TGAI. Only the analyses for 4 batches are reported.

- Petitioner must submit a revised CSF for ACCENT™ Technical (352-LGL). The certified lower limit of [redacted] is stated incorrectly on CSF dated 2/13/90.

62-3: Analytical methods to verify certified limits (40 CFR 158.180)

The petitioner has submitted analytical methodology (Method No. ESB-30-88, "ACCENT™ (DPX-V9360), Technical and Formulation Determinations of DPX-V93260, Reversed-Phase Liquid Chromatographic (RPLC) Assay Method" dated 11/18/88, MRID#409545-10) for the quantitative determination of DPX-V9360 in the 75% granular formulation.

[redacted]

The analytical methodology used for determination of potential impurities in the TGAI and ACCENT™ are discussed in the Confidential Appendix.

DEB Commments/Conclusions

The submitted analytical enforcement methodology for certified limits is adequate. No additional data are needed.

63-2 to 63-13: Physical and Chemical Characteristics (40 CFR 158.190):

Methods used to meet the requirements of Guidelines Reference Nos. 63-2 through 63-13 for the technical product shall be referenced or described in the application for registration.

63-2:	Color	white
63-3:	Physical State	soild
63-4:	Odor	paste-like

63-5: Melting Point — 141-144°C

63-6 Boiling Point — Not applicable

63-7: Density — 0.313 g/ml

63-8: Solubility

solvent	solubility limit*
pH 5.0 buffer	.04
pH 7.0 buffer	1.2
pH 9.0 buffer	3.9

* (g/100 g buffer at 25°C)

solvent	solubility limit†
acetone	18
acetonitrile	23
benzene	2.7, 1.7*
chloroform	64
N,N dimethylformamide	64
ethanol	4.5
ehtyl acetate	3.8
n-hexane	<0.02
methanol	0.44
methylene chloride	160
2-propanol	1.2
tetrahydrofuran	2.6, 26*
toluene	0.37
xylenes	0.20

† (ppm x 10^3 at 28 ± 1°C)
* Clarification needed from registrant

63-9: Vapor Pressure: 1.2×10^{-16} torr

63-10: Dissociation Constant: pK_a value = 4.3 (acid)

63-11: Octanol/water partition coefficient:

pH 5	0.44
pH 7	0.017
pH 9	0.01

63-12: pH: A slurry in HPLC water caused the pH of the water to decrease from 6.6 to 4.5

63-13: Stability: The TGAI is solution stable in the presence of iron metal and ferrous (Fe^{+2}. The solid TGAI is stable under normal storage at 25°C and at 45°C for 3 weeks.

DEB Comments/Conclusions

Data on the TGAI has been submitted for Guidelines Reference Nos. 63-2 through 63-13 (MRID#'s 409545-01 and 409242-03). Additional data are needed for the TGAI, DPX-V9360.

° The petitioner must clarify the correct solubilities. Solubilities are listed for DPX-V9360 in benzene and tetrahydrofuran as 2.7 and 2.6, respectively, in MRID#409545-01, but as 1.7 and 26, respectively, in MRID#409242-03.

PRODUCT CHEMISTRY

for

nicosulfuron

(DXP-V9360)

Confidential Appendix

61-2: Beginning Materials and Manufacturing Process

The petitioner has submitted ingredient names, the producers of beginning materials, and specification sheets for such in MRID#409545-01.

[redacted]

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

DEB Comments/Conclusions:

The purities of the beginning materials are adequately discussed and sufficient data have been submitted (MRID#409545-01) to the Agency. No additional data are needed.

The manufacturing process is adequately discussed. (MRID#409545-01) No additional data are needed.

61-2: Description of Formulation Process

A discussion of the formulation of ACCENT™ has been submitted (MRID#409242-01):

[redacted]

DEB Comments/Conclusions:

The petitioner has submitted adequate data in regards to the identification of the ingredients and subsequent technical specifications of each. The submitted description of the formulation process is adequate. The petitioner has also discussed the quality control measures/checks in the daily production of formulated lots. No additional discussion is required for the formulation process.

61-3: Discussion of the Formation of Impurities

The petitioner has submitted a discussion of the formation of [redacted] impurities, and the residues of [redacted]

DEB Comments/Conclusions:

Data have been submitted in regards to the formation of possible impurities in the production of DPX-V3960. The technical grade active ingredient (TGAI) can have [redacted] impurities. Additional discussion is in Section 62-1.

Page _____ is not included in this copy.

Pages 15 through 16 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

__✓__ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

DEB Comments/Conclusions:

Partial data have been submitted for identification and/or analysis of possible impurities in the production of DPX-V9360. (MRID#409545-01). Additional data are needed.

- Petitioner must provide the Chemical Abstracts chemical reference numbers (CAS#'s) for all impurities listed, if and/or when available that are potentially present in the TGAI.

- Petitioner must report the analysis of one additional production batch.

- Petitioner must submit a revised CSF for ACCENT™ Technical (352-LGL). The certified lower limit of impurity [redacted] is stated incorrectly on CSF dated 2/13/90.

62-2: Certification of Ingredient Limits:

Composition of Manufacturing Products

The petitioner has submitted the composition of the ACCENT™ formulation: (MRID#409242-01).

[redacted]

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Table cont'

[redacted]

DEB Comments/Conclusions:

Adequate data has been submitted for this requirement. No additional data are necessary.

62-3: Analytical Methods to Verify the Certified Limits:

The a.i. can be determined by a reverse phase HPLC method, DuPont Method ESB-30-88.

[redacted] The petitioner has submitted analytical conditions and sample charts for all methods submitted (MRID#409545-01).

DEB Comments/Conclusions:

Adequate data has been submitted for this requirement. No additional data are necessary.

DATA REQUIREMENTS FOR Nicosulfuron (DPX-V9360) TECHNICAL PRODUCTS[1/] (EPA REG. NO. 352-LGL; E. I. du Pont de Nemours & Company, Inc.)

Table A

Data Requirement	Composition[2/]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Time Frame For Submission
158.150, 158.160, 158.162, 158.167, 158.170, 158.175, 158.180, and 158.190 Product Chemistry					
Product Identity and Composition:					
61-1 - Product Identity and Disclosure of Ingredients	TGAI	Yes	MRID #409545-01	No	
61-2 - Description of Beginning Materials and Manufacturing Process	TGAI	Yes	MRID #409545-01	No	
61-3 - Discussion of Formation of Impurities	TGAI	Yes	MRID #409545-01	No	
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	TGAI	Partially	MRID #409545-01	Yes	
62-2 - Certification of Ingredient Limits	TGAI	Partially	MRID #409545-01	Yes	
62-3 - Analytical Methods to Verify Certified Limits	TGAI	Yes	MRID #409545-01	No	

DATA REQUIREMENTS FOR Nicosulfuron (DPX-V9360) TECHNICAL PRODUCTS[1/] (EPA REG. NO. 352-LGL; E. I. du Pont de Nemours & Company, Inc.)

Table A (Continued)

Data Requirement	Composition[2/]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Time Frame For Submission
Product Chemistry (continued)					
Physical and Chemical Characteristics					
63-2 - Color	TGAI	Yes	MRID #409545-01	No	
63-3 - Physical State	TGAI	Yes	MRID #409545-01	No	
63-4 - Odor	TGAI	Yes	MRID #409545-01	No	
63-5 - Melting Point	TGAI	Yes	MRID #409545-01	No	
63-6 - Boiling Point	TGAI	NA	MRID #409545-01	No	
63-7 - Density, Bulk Density or Specific Gravity	TGAI	Yes	MRID #409545-01	No	
63-8 - Solubility	TGAI or PAI	Partially	MRID #409545-01	Yes	
63-9 - Vapor Pressure	TGAI or PAI	Yes	MRID #409545-01	No	
63-10 - Dissociation Constant	TGAI or PAI	Yes	MRID #409545-01	No	
63-11 - Octanol/Water Partition Coefficient	PAI	Yes	MRID #409545-01	No	
63-12 - pH	TGAI	Yes	MRID #409545-01	No	
63-13 - Stability	TGAI	Yes	MRID #409545-01	No	
Other Requirement					
64-1 - Submittal of Samples	TGAI and PAI	Partially		Yes[3/]	

1/The chemical name for DPX-V9360 (ACCENT™) is 3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl) aminocarbonyl)aminosulfonyl))-N,N-dimethyl. The common name is nicosulfuron (ISO approved, ANSI proposed).

2/Composition: TGAI = technical grade active ingredient; PAI = pure active ingredient

3/Only the PAI has been submitted; a sample of TGAI must be submitted.

RESIDUE CHEMISTRY

Introduction

The Residue Chemistry Requirements as given in 40 CFR 158.240 which explains the minimum data the Agency will need to adequately assess the residue chemistry of DPX-V9360 (nicosulfuron, ACCENT™).

There are, as yet, no permanent tolerances for DPX-V9360 on any raw agricultural commodities [including livestock meat, fat, meat byproducts (including liver and kidney), milk, or eggs], or any processed commodities. DEB has recently recommended in favor of a Section 18 (1/25/90) for use on field corn. Temporary 0.1 ppm tolerances have been recommended for corn forage, silage, fodder, and grain. In accordance with 40 CFR 180.6(b) DEB determined that no tolerances would be needed for livestock (including poultry) meat, fat, meat byproducts (including liver and kidney), milk and/or eggs for the Section 18.

171-2: Chemical Identity: Manufacture and Formulation

According to 40 CFR 158.240, Guidelines Reference No. 171-2, the same information required under 40 CFR 158.150, -.155, -.160, -.162, -.165, -.167, -.170, -.175, -.180, and -.190 is required for the proposed herbicide ACCENT™. The active ingredient (a.i.) DPX-V9360, nicosulfuron, is 3-pyridinecarboxamide, 2-((((4,6-dimethoxy-pyrimidin-2-yl) aminocarbonyl)aminosulfonyl))-N,N-dimethyl and is formulated as a granular, water dispersible product. The manufactured a.i., DPX-V9360, is certified to have 88.5% minimum purity. Additional data are required for Section A in regards to product chemistry. (See the included product chemistry chapter and its Confidential Appendix for a discussion of additional data requirements.)

171-3: Directions For Use: Proposed Use

According to 40 CFR 158.240, Guidelines Reference No. 171-3, information is required for crops to be treated, rate of application, number and timing of applications, preharvest intervals, and revelant restrictions.

The product is applied by broadcast postemergent over-the-top application when the corn is in the 2- to 6-leaf stage. A second application may be applied postemergent directed to weeds prior to the 10-leaf stage (ca. 14-28 days after first application). The proposed application rates are 1 1/3oz ACCENT™/A/season (1oz (0.0625lb) a.i./A/season) dependent upon the weed species and its size at the time of application. Split applications are recommended at 2/3oz plus 2/3oz ACCENT™/A (0.5 oz a.i/A). The second 2/3oz goes on 14-28 days after the first application. Directions suggest a minimum of 10 gallons for the proposed application rates. The label states that applications should be made by ground equipment only. Label restrictions include 1)"Do not apply ACCENT™ to soils having a pH higher than 7.5 because injury

to any rotational crop other than field corn may result", 2) "Do not apply to popcorn, sweet corn or corn grown for seed production", 3) "Single or split applications of ACCENT™ may not exceed a total of 1 1/3oz/A in any one crop year", 4) "Do not graze or feed forage or grain from the treated areas to livestock within 30 days after applications of ACCENT™".

Rotational crop restrictions are dependent upon the US location and the soil pH: winter cereals, 3-15 months; field corn, anytime; soybeans, 8 months; spring cereals, 8-18 months; alfalfa, 9-15 months; clover, 9-15 months;dry beans, 8-20 months, and sorghum, 9-20 months. Alfalfa, clover, dry beans, and sorghum require a field assay in selected states if the soil pH >7.0. For other crops not listed a field bioassay is recommended before planting.

Rotational crop restrictions listed above may not be acceptable according to Agency policy (See memo of 1/14/87 E. Tinsworth, RD) in regards to rotational crops after application of a pesticide. The Environmental Fate and Ground Water Branch in EFED should be made aware of these restrictions.

171-4: Nature of the Residue

In Plants:

A single metabolism study has been submitted for 14C-DPX-V9360 in corn (MRID#410826-26) in this petition. Both [pyridine-2-14C]-DPX-V9360 (sp. act. 62.9 uCi/mg, 98% radiochemical purity determined by TLC and HPLC) and [pyrimidine-2-14C]-DPX-V3960 (sp. act. 62.2 uCi/mg, 99% radiochemical purity determined by TLC and HPLC) were applied postemergence to greenhouse-grown, pot-contained field corn at the 4-5 leaf stage (14-15 inches high) as an over-the-top aqueous spray. The application rate was 70 g a.i./ha (1 oz. a.i./A), the maximum proposed use rate. The soil was representative of a US corn growing region, and a typical field corn, Cargill 937, was used. Watering, fertilizing, and application of other pesticides were recorded. Twelve additional pots were divided into two groups and an application equivalent to 140 g a.i./ha (2.0 oz a.i./A, 2X maximum use rate) of either 14C-labelled DPX-V9360 was made for preparative purposes. Some phytotoxicity was observed. Whole plant samples were gathered after the spray dried at days 0, 7, 14, and 30. Silage samples were taken at 49 days and grain, cob, and stalk (stover) samples were collected at 113 days (maturity). The fresh weights of all samples were recorded, some of the plants were rinsed by an acetone:water solution to remove surface 14C-residues (whole plants only from days 0, 7, 14, and 30; silage and mature corn were not rinsed), and the samples (unrinsed plants, rinsed plants, and aqueous solutions from rinsed plants) were stored frozen at -20°C until analysis.

The plants, as well as the solutions, were analyzed by HPLC equipped with UV and radiochemical detectors. In some cases, radiochromatograms were reconstructured from eluted fractions

using specialized computer software. TLC was used as a confirmatory method for chemical purity and analysis of plant samples. The radiochemical impurities included the hydrolysis products, pyridine sulfonamide (present in [pyridine-2-14C] DPX-V9360) and pyrimidine amine (present in [pyrimidine-2-14C] DPX-V9360).

The quantitation and distribution of total radioactivity were determined using unrinsed lyophilized plant samples. After combustion the collected 14C-CO_2 was measured by LSC and the levels are listed as follows:

PHI, in days	Crop Fraction	Concentration in ppm[a]	
		Pyridine-2-14C	Pyrimidine-2-14C
0	whole plant	4.3	3.3
7	" "	1.3	0.09
14	" "	0.21	0.26
30	" "	0.014	0.006
49	silage	0.005	0.003
113	grain	0.002	0.003
113	cobs	0.004	0.004
113	fodder (grain, cobs, & stalk)	0.065	0.058
113	stover	0.096	0.075

[a] DPX-V9360 equivalents based on fresh plant weight

All the above corn commodities, i.e., 30-day forage, silage, and fodder were extracted to characterize the 14C-residues; grain and cobs were not extracted since the total 14C-levels were so low. The extraction procedure was validated by adding 14C-pyridinyl or -pyrimidinyl DPX-V9360 to the extraction solution and running through the procedure, with a final analysis by HPLC. The various whole plants and plant parts were extracted with an acetone:dilute ammonium carbonate solution, and the extracts were analyzed by HPLC and TLC. The extracted plant material was air-dried and stored frozen until combusted for the determination of unextractable 14C-residues. All samples contained unextractable 14C-levels <10% TRR or <0.1 ppm (DPX-V9360 equivalents). An aliquot of this material was also checked for bound 14C-residues by enzymatic hydroylses, e.g., a cellulase and a glucosidase. Stover samples released 46% of bound 14C-residues while stover samples were also exhaustively extracted, and >60% of bound 14C-residues were released. The use of glucosidase confirmed the presence of a hydroxylated metabolite, i.e., a 5'-O-glucoside

as shown by HPLC and TLC analyses. Using HPLC and TLC, the major metabolites were determined by comparsion of unlabelled reference standards. The following tables give the results of the analyses, and the structures of the metabolites.

Concentration of DPX-V9360 & Metabolites in Corn Treated with [Pyridine-2-14C]DPX-V9360

	Total PPM (eq of DPX-V9360)[a]					
Compound	Day 0	7	14	30[b]	49	113[c]
DPX-V9360	3.17	0.67	0.074	0.003	0.0005	0.008
5'-Hydroxy DPX-V9360	0.027	0.011	0.001	ND	ND	ND
5'-O-Glucoside DPX-V9360	0.014	0.035	0.005	ND	ND	ND
Compound C	0.16	0.027	0.006	ND	ND	ND
Pyridine Sulfonamide	0.17	0.31	0.063	0.005	0.002	0.038
Compound A	0.31	0.047	0.008	ND	ND	ND
DPX-V9360 Carboxamide	ND	ND	ND	ND	<0.0005	ND
Polar (undefined)	ND	ND	ND	0.002	ND	ND
Total	3.9	1.2	0.15	0.010	<0.003	<0.03

a Total from rinsed and/or extracted 14C-residues; % nonextractable 14C-residue: 1.2 (day 0), 3.1 (day 7), 8.8 (day 14), 12.5 (day 30), 41.8 (day 49), and 18.5 (day 113). Maximum unextracted equivalent parent was reported as 0.051 ppm on 0 day.

b Proposed PHI.

c Only stalk was extracted. The grain and cobs each contained <0.005 ppm total 14C-equivalents and were not extracted.

Concentration of DPX-V9360 & Metabolites in Corn Treated with [Pyrimidine-2-14C]DPX-V9360

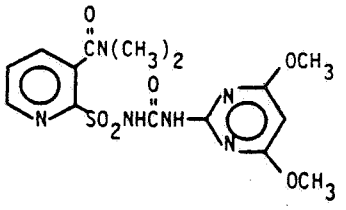
	Total PPM (eq of DPX-V9360)[a]					
Compound	Day 0	7	14	30[b]	49	113[c]
DPX-V9360	2.36	0.63	0.093	0.001	<0.0005	0.021
5'-Hydroxy DPX-V9360	0.28	0.008	0.001	<0.0005	<0.0005	ND
5'-O-Glucoside DPX-V9360	0.015	0.037	0.010	<0.0005	<0.0005	ND
Compound C	0.13	0.019	0.007	ND	ND	ND
Compound B	ND	0.009	0.004	ND	ND	ND
Compound A	0.18	0.034	0.011	ND	<0.0005	ND
Pyrimidinyl Urea	ND	0.020	ND	ND	ND	ND
Polar B	ND	ND	ND	<0.0005	ND	ND
Polar A	0.024	0.044	0.019	0.001	<0.0005	0.012
Total	3.0	0.80	0.15	<0.004	<0.0025	0.033

a Total from rinsed and/or extracted 14C-residues; % nonextractable 14C-residue: 2.4 (day 0), 5.6 (day 7), 17.3 (day 14), 23.0 (day 30), 51.6 (day 49), and 33.0 (day 113). Maximum unextracted equivalent parent was reported as 0.076 ppm on 0 day.

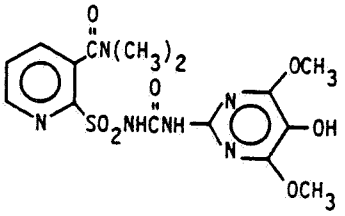
b Proposed PHI.

c Only stalk was extracted. The grain and cobs each contained <0.005 ppm total 14C-equivalents and were not extracted.

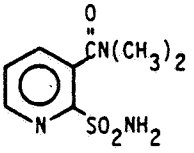
Structures of Parent and Metabolites



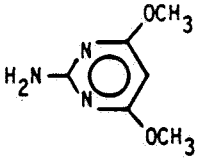
1. DPX-V9360
2. 2-[[[[(4,6-Dimethoxy-pyrimidin-2-yl)amino]carbonyl]amino]sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide



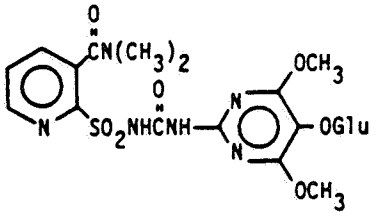
1. 5'-Hydroxy DPX-V9360
2. 2-[[[[(4,6-Dimethoxy-5-hydroxy-pyrimidin-2-yl)amino]carbonyl]amino]-sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide



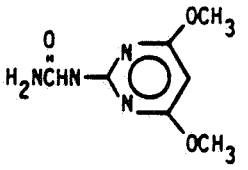
1. Pyridine Sulfonamide
2. 2-Aminosulfonyl-N,N-dimethyl-3-pyridinecarboxamide



1. Pyrimidine Amine
2. 2-Amino-4,6-dimethoxypyrimidine



1. DPX-V9360-5'-O-Glucoside
2. 2-[[[[(4,6-Dimethoxy-5-glucosyl-pyrimidin-2-yl)amino]carbonyl]amino]-sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide



1. Pyrimidinyl Urea
2. N-(4,6-dimethoxy-2-pyrimidinyl)urea

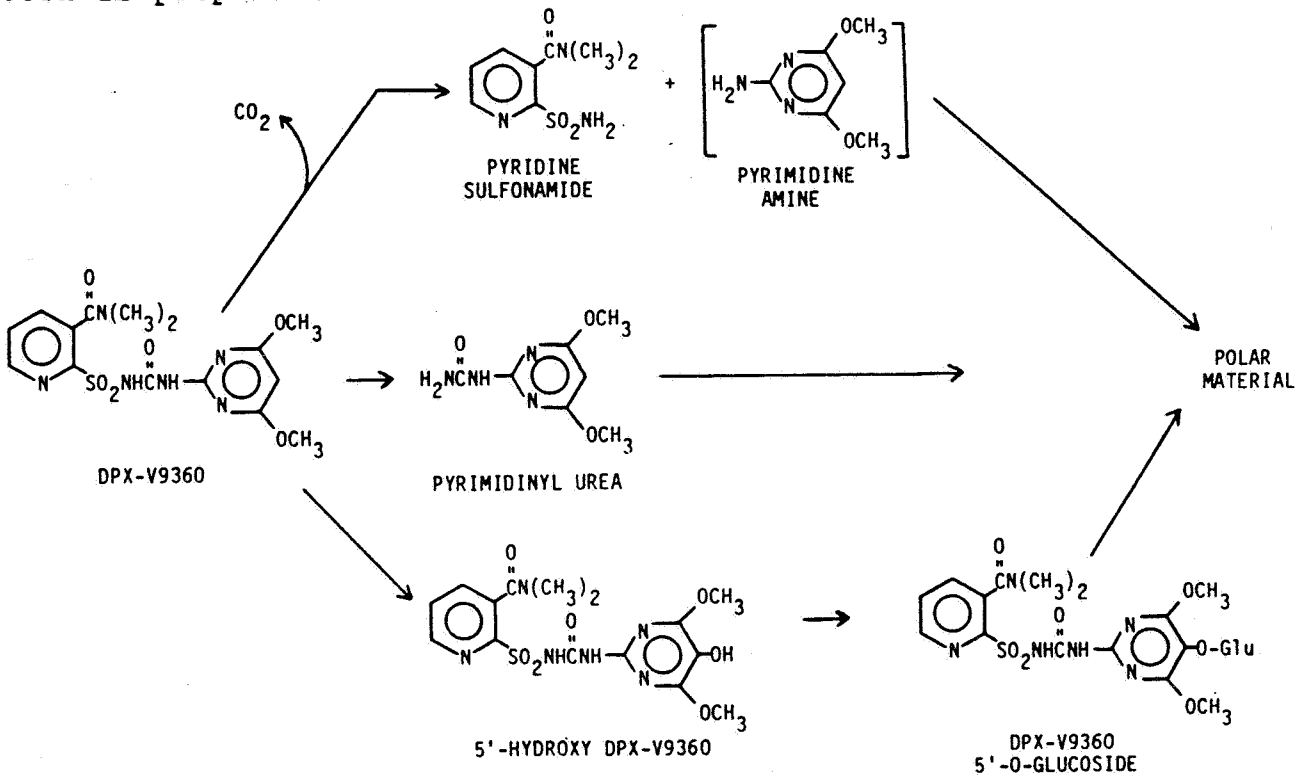
For [pyridine-2-14C]DPX-V9360-treated corn, the total level of 14C in 30-day forage samples was 0.014 ppm (combustion, DPX-V9360 equivalents). Extraction of this residue gave 0.003 ppm DPX-V9360 and 0.005 ppm metabolite pyridine sulfonamide (determined by HPLC analyses of rinsings and extracts). Approximately 0.002 ppm are undefined polars (HLPC and TLC analyses) and 0.001 ppm nonextractables. The other corn commodities, i.e., silage (49 days PHI), fodder (113 days PHI), and stover (113 days PHI), were 0.005, 0.065, and 0.096 ppm (DPX-V9360 equivalents), respectively.

For [pyrimidine-2-14C]DPX-V9360-treated corn, the total level of 14C in 30-day forage samples was 0.006 ppm (combustion, DPX-V9360 equivalents). Extraction of this residue gave 0.001 ppm DPX-V9360 and <0.0005 ppm metabolites 5'-OH-DPX-V9360 and 5'-O-glucoside DPX-V9360 (determined by HPLC analyses of rinsings and extracts). Approximately 0.001 ppm are undefined polars (HPLC and TLC analyses) and <0.0005 ppm nonextractables. The other corn commodities, i.e., silage (49 days PHI), fodder (113 days PHI), and stover (113 days PHI), were 0.003, 0.058, and 0.075 ppm (DPX-V9360 equivalents), respectively.

Several compounds, i.e, A, B, C, Polar (undefined), Polar A, and Polar B remain undefined in the study, but all are <10% TRR or are not detected at the 30-day forage, silage, or mature corn commodities. In addition, the very low levels will make it difficult to adequately characterize these unknowns.

Based upon the results, the metabolism of DPX-V9360 proceeds predominantly via two mechanisms: the hydrolysis of the sulfonylurea bridge yielding pyridine sulfonamide and pyrimidine amine, and the hydroxylation of DPX-V3960 at the 5-position of the pyrimidine amine followed by glucosidation (in early forage samples). The glucose conjugate and its aglycon were present in the whole plant (49 day PHI), but were not present in the fodder or stover (113 day PHI). The grain and cob (113 day PHI) were not analyzed since these contained <0.005 ppm total 14C-equivalents of DPX-V9360. Pyridine sulfonamide was present in the whole plant (0 to 30 day PHI) and in silage (49 day PHI), and fodder and stover (113 day PHI). Again the grain and cob were not extracted because of very low total 14C-residues.

The following metabolic pathway of nicosulfuron (DPX-V9360) in corn is proposed:



The analyses show that the parent DPX-V9360 gradually decreases during the corn growing season and is present in very low levels at maturity. However, residues of metabolite pyridine sulfonamide begin at day 0 and are detected in the whole plant and stalk at maturity (113 day PHI). These residues are higher than the detected residues of the parent DPX-V9360. Pyrimidine amine is further metabolized to the 5-OH DPX-V9360 and its glucoside, but are not detected in the whole plant (49 day PHI) or in fodder or stover (113 day PHI).

The parent DPX-V9360 is hydrolyzed rapidly in acidic soils with the formation of pyridine sulfonamide and pyrimidine amine as the metabolites. Note: The pH of the soil used in this metabolic study is not given. The petitioner must submit the soil pH. These metabolic soil residues can be adsorbed by the root system and appear in the corn plant at harvest. In fact, pyridine sulfonamide appears to be present in the corn stalk and whole plant at a 113-day PHI.

Therefore the primary residue of regulatory concern is the parent DPX-V9360. The petitioner has been requested to submit additional field residue data (See Residue Data Section, this memo) for the metabolite pyridine sulfonamide and this data must be reviewed before DEB can determine if pyridine sulfonamide should be included in the tolerance expression.

In animals:

The petitioner has submitted the following rat metabolism study:

"Metabolism of [Pyridine-2-14C] and [Pyrimidine-2-14C] DPX-V9360 by the Laboratory Rat" (MRID#410826, DuPont Report AMR #911-87).

Five groups of rats, 5 males and 5 females, were dosed with either [pyridinyl-14C]-DPX-V9360, sp. act. 62.9 uCi/mg, 99.0% radiochemical purity, or [pyrimidinyl-14C]DPX-V9360, sp. act. 62.2 uCi/mg, >98% radiochemical purity. The groups were given doses as follows: one received an oral dose of 10 mg/kg [pyridine-2-14C]DPX-V9360; another received a 10 mg/kg [pyridine-2-14C]DPX-V9360 intravenous dose; a third received an oral 10 mg/kg [pyridine-2-14C]DPX-V9360 dose, but only after the animals had received a 10 mg/kg daily dose of non-radioactivity DPX-V9360 for 14 days; the fourth group received a single high oral dose of 1000 mg/kg [pyridine-2-14C]DPX-V9360; the fifth group received an single oral dose of 1000 mg/kg [pyrimidinyl-14C] DPX-V9360. All animals were sacrificed 96 hours after dosing and tissues were collected for radioactive analyses. Urine and feces samples were analyzed for total radioactivity.

Percentages of dose recovered[a]

Treatment level, mg/kg, interval	male urine	male feces	male carcass &tissues	female urine	female feces	female carcass &tissues
[pyridine-2-14C] DPX-V9360						
10.0, oral	20	80	<0.1	14	88	<0.2
1000, oral	9	89	<0.1	10	94	<0.2
10.0, intravenous	76	30	<0.4	80	27	<0.5
10.0, oral (after multiple dose)	13	87	0.1	19	85	<0.3
[pyrimidine-2-14C] DPX-V9360						
1000, oral	11	92	<0.1	9	95	<0.1

[a] Average for five rats (both male or female values)

Examination of these results show that both males and females excreted essentially all of the radionuclide in the feces and urine. Elimination of 14C-CO_2 was not observed. Little uptake was observed in the animal tissues.

Feces and urine samples in which the rats were administered either of the 14C-labelled-DPX-V9360 compounds, were analyzed by HPLC and TLC, and unknowns were isolated and characterized (See table below). No organ or tissue showed total 14C-radioactivity >0.01 of the admimistered dose. The major radioactivity was recovered as the parent which ranged from 85 to 97%. Two metabolites, pyridine sulfonamide and 5-hydroxy pyrimidine amine, were identified. The presence of pyridine acid sulfonamide was also suggested, but not positively identified; metabolites MU "A" (tentatively assigned as pyridine acid sulfonamide) and MF #1 are suggested to be the identical compounds. No structure has been proposed for MF "A". These undefined metabolites makeup <10% TRR. No attempt was made to characterize the residues in the body tissues (including liver or kidney) other than measure the total 14C-radioactivity, because the total carcass uptake of 14C-residues was minimal, even for the high 1000 ppm dose.

Based on the metabolites identified, the major pathway in the rat is cleavage of the parent DPX-V9360, to yield pyridine sulfonamide and pyrimidine amine; 5-OH pyrimidine amine could be formed either before or after the cleavage.

Percent Distribution of Metabolites in Pooled Raw Samples[a]

Identified Residue	Male urine/feces		Female urine/feces	
	pyridinyl[b]	pyrimidinyl[c]	pyridinyl	pyrimidinyl
DPX-V9360 (parent)	11(70)/80 (19)	9/89	11(71)/82 (20)	7/91
pyridine sulfonamide	3/--	--	1/--	--
5-OH pyrimidine amine[d]	--	2/--	--	2/--
Others,				
MU "A"[e] (urinary)	(0.7)/--	--	0.5(2.4)/--	--
MF "A"[f] (fecal)	--/(1.3)	--	--/2.1(3.1)	--
MF #1[g] (fecal)	--/8.2(7.5)	--	--/5.2(1.8)	--

Table cont'

a The total recovery of the dose ranged from 87 to 113%.

b Values are the average for animals dosed with 10 mg/kg, 1000 mg/kg, and 10 mg/kg (after multiple dose); values in () are for i.v. dose of 10 mg/kg.

c Values are for animals dosed with 1000 mg/kg.

d Only reported for animals dosed with [pyrimidine-2-14C]DPX-V9360.

e Reported only for animals dosed with 10 mg/kg (after multiple dose and i.v) [pyridine-2-14C] DPX-V9360.

f Reported only for animals dosed with 10 mg/kg (oral and i.v.).

g Reported only for animals dosed with 10 mg/kg and 1000 mg/kg (oral) and 10 mg/kg (i.v.).

The petitioner has submitted the following goat metabolic study,

"Metabolism of [Pyrimidine-2-14C]DPX-V9360 and [Pyridine-2-14C] DPX-V9360 in Lactating Goats" (MRID#410826-27, DuPont Report #AMR-947-87):

Two female goats weighing 43 kg (#1) and 34 kg (#2) (1.4 and 1.8 mg/kg bodyweight respectively), were dosed daily for 3 consecutive days in feed rations treated with [pyrimidine-2-14C]DPX-V9360, sp. act., 62.2 uCi/mg, radiochemical purity, >95%, isotopic purity, 97%, and [pyridine-2-14C]DPX-V9360, sp. act., 62.9 uCi/mg, radiochemical purity, >95%, isotopic purity, >99%, respectively. Dosing capsules were prepared with the 14C-labelled materials, 13C-enriched isomers (C2 position of each respective ring), and nonradioactive DPX-V9360. The capsules were analyzed prior to dosing by LSC for total C14-activity and by HPLC for chemical analysis. These capsules were imbedded in a larger gelatin capsule containing 6 g of goat chow. Goat #1 was housed for a 9-day acclimation period, while goat #2 was kept for 11 days. Both goats showed good health and milk production before and during dosing. The dosage represents a daily feeding level of approximately 60 ppm based on the average feed and hay consumption of 1 kg/day. Samples of milk, bile, urine, and feces were collected daily and analyzed by combustion/liquid scintillation counting. A control goat was not used in the study. Milk, bile, urine, and feces were collected at least one day prior to dosing for use as control samples. After treatment commenced all samples were collected and frozen until analysis. Within 24 hours after the last dose, the animals were sacrificed and the tissues and organs were rinsed free of blood and stored frozen in plastic bags.

14C Residues in Elimination Products, Milk, and Tissues of Goats Dosed With 14C-Labelled DPX-V9360 For 3 Consecutive Days

		[Pyridine-2-14C]DPX-V9360			[Pyrimidine-2-14C]DPX-V9360		
Sample	Day	Total uCi	Conc of Total 14C Residues in ppm [a]	% of Total Dose[b]	Total uCi	Conc of Total 14C Residues in ppm [a]	% of Total Dose[b]
Milk	1	ND[c]	ND	--	0.03	0.02, 0.01[d]	0.01
	2	ND	ND	--	0.06	0.03, 0.02	0.03
	3	ND	ND	--	0.07	0.03, 0.02	0.03
Urine	1	8.4	10.5	4.0	6.2	2.6	2.9
	2	10.8	23.6	5.2	14.6	8.2	6.8
	3	12.7	12.6	6.1	15.8	10.2	7.3
Feces	0	0.1	0.13	0.05	0.09	0.1	0.04
	1	25.9	38.6	12.5	4.1	3.9	1.9
	2	50.6	55.7	24.3	30.8	31.9	14.3
	3	56.7	56.5	24.3	33.6	31.8	15.6
Bile	1	0.31	3.2, 1.8[d]	0.2	0.03	0.03, 0.5[d]	0.02
	2	0.06	3.4, 2.8	0.3	0.06	0.85, 1.4	0.03
	3	0.46	2.3, 2.6	0.2	0.19	0.95, 0.79	0.09
Liver	--	0.09	0.1	0.04	0.06	0.05	0.03
Kidney	--	<0.01	0.07	<0.01	<0.01	0.05	<0.01
Fat (total)	--	0.01	0.01 - 0.03[e]	f	0.02	0.005 - 0.02[e]	f
Muscle (total)	--	ND	0.01 - 0.02	f	<0.01	0.001 - 0.01	f

a Calculated as ppm of [pyridine-2-14C] or [pyrimidine-2-14C]DPX-V9360, respectively.
b Each capsule contained ca. 30 mg 14C-labelled DPX-V9360 (34.6 uCi, pyridinyl; 35.8 uCi, pyrimidinyl). Total dose 180 mg. Goat #1, pyridinyl label, goat #2, pyrimidinyl label.
c None detected. LSC results from counting aliquots were less than twice the background, and not quantifiable.
d Morning sample, evening sample.
e Range for back, omental, prepheral, and renal samples.
f Total tissues were not taken, thus, data is not available.

Aliquots of each milk, urine, and bile sample were analyzed for total 14C-activity by LSC. All tissues, organs, and feces of the goat dosed with either 14C-label were homogenized, combusted, and the released $14CO_2$ trapped and measured by LSC.

Radiochromatograms were constructed using specialized computer software to plot the net dpm for each HPLC fraction versus time.

Residues continued to increase in the milk up to day 3 for the pyrimidinyl-labelled DPX-V9360 (this is a possible plateau at or soon after day 3), while the pyridinyl-labelled DPX-V9360 gave no detectable 14C-residues on day 1, 2, or 3. The total 14C-activity measured in milk (pyrimidinyl-labelled) by combustion/LSC was a maximum of 0.03 ppm (0.03% TRR).

The administered 14C-dosage was excreted in the urine at 46% and 17%, and in the feces at 62% and 32%, respectively for the pyridinyl- and pyrimidinyl-labelled DPX-V9360. Uptake of residues was low for all tissues and organs for either label. The highest level, 0.1 ppm (0.04% of total dose) was in the liver from the goat treated with the pyridinyl label. All other tissues had TRR of approximately 0.07 ppm or less (DPX-V9360 equivalents). Radioactivity in the collected bile comprised 0.1% and 0.7% of the total dose, respectively for the pyridinyl- and pyrimidinyl-labelled DPX-V9360.

Isolation and identification of 14C-residues were achieved by use of HPLC and TLC, and LC/MS. The HPLC elution of radioactivity was monitored with a radiochemical detector. Radioactive compounds were compared to retention times to those of cochromatographed reference standards that were monitored by a UV detector. The incorporation of 13-labelled DPX-V9360 (ca. 40% level) facilitated the mass spectral analyses of the metabolite from the sample impurities.

Metabolite Characterization in Tissues, Milk, and Excreta from Lactating Goats Treated at ca. 60 ppm/day with [Pyridinyl-2-14C]DPX-V9360.[a]

Commodity	Total ppm	Parent	Metabolite					Not Characterized
			N1	N2	N3	N4	N5	
Liver	0.1	--	--	--	--	--	--	100%
Kidney	<0.1	--	--	--	--	--	--	100%
Milk	ND	--	--	--	--	--	--	--
Bile	16.1[b]	84%[c]						16%
Urine[d]	46.7[e]	75%	3%	<2%	5%	3%	<10%	<3%
Feces	151[e]	90%[f]	--	--	--	--	--	<10%

Table cont'

[a] Approximately 48% of the total dose (180 mg) was recovered.

[b] Three day total for 6 samples, ranging from 1.8 to 3.4 ppm (DPX-V9360 eq.).

[c] Evening sample, day 2.

[d] Percentages of recovered parent and metabolites are averages from day 2 and day 3 samples.

[e] Three day total.

[f] Evening sample of day 3 only.

ND : none detected

Metabolite Characterization in Tissues, Milk, and Excreta from Lactating Goats Treated at ca. 60 ppm/day with [Pyrimidinyl-2-14C]DPX-V9360.[a]

Commodity	Total ppm	Parent	Metabolite M1	Not Characterized
Liver	0.05	<50%	--	>50%[b]
Kidney	0.05	--	--	100%
Milk	0.01 - 0.02[c]	--	--	100%
Bile	4.5[d]	84%[e]	--	16%[e]
Urine	21[d]	71%	15%	14%[b]
Feces	68[d]	89%	--	11%

[a] Approximately 80% of the total dose (180 mg) recovered.

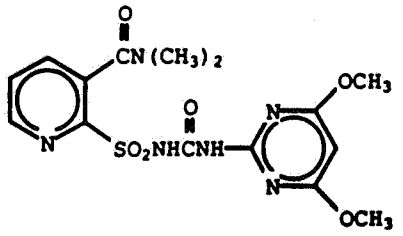
[b] Comprised of numerous peaks by HPLC analysis, but not analyzed further.

[c] Three-day total, 0.13 ppm (DPX-V9360 eq.).

[d] Three-day total.

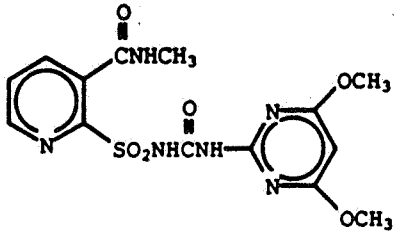
[e] Evening sample, day 2.

The frozen excreta and tissues were extracted and processed through an ion-exchange resin clean-up, followed by HPLC fractionation and separation as the major isolation and purification technique of the metabolite for either 14C-labelled material.



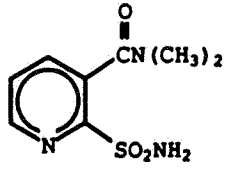
1. DPX-V9360
2. 2-[[[[(4,6-Dimethoxy-pyrimidin-2-yl)amino]carbonyl]amino]-sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide

N1



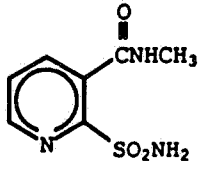
1. N-Desmethyl DPX-V9360
2. 2-[[[[(4,6-dimethoxy-pyrimidin-2-yl)amino]carbonyl]amino]-sulfonyl]-N-methyl-3-pyridinecarboxamide

N3



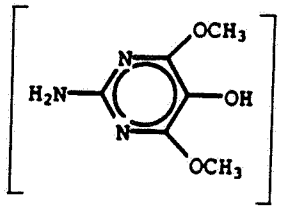
1. Pyridine Sulfonamide
2. 2-Aminosulfonyl-N,N-dimethyl-3-pyridinecarboxamide

N4



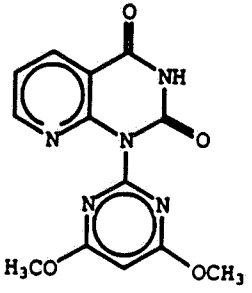
1. N-Desmethyl Pyridine Sulfonamide
2. 2-(Aminosulfonyl)-N-methyl-3-pyridinecarboxamide

M1



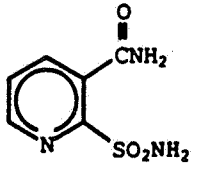
1. 5-Hydroxy Pyrimidine Amine, polar conjugate of
2. 2-Amino-4,6-dimethoxy-5-hydroxypyrimidine

N2

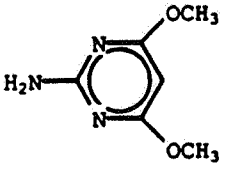


1. V9360 Cyclized Ipso Compound
2. 1-(4,6-dimethoxy-pyrimidin-2-yl)pyrido[2,3-d]pyrimidine-2,4-(1H,3H)-dione

N5



1. Pyridine Sulfonamide Carboxamide
2. 2-(Aminosulfonyl)-3-pyridinecarboxamide



1. Pyrimidine Amine
2. 2-Amino-4,6-dimethoxypyrimidine

Raw urine from the goat treated with the 14C-pyridinyl (#1) was eluted from a resin column into 3 fractions. The majority of 14C-activity was present in one fraction and HPLC analysis of this fraction gave parent plus 5 metabolites (N1, N2, N3, N4, and N5). Only 3% of the 14C-activity was in the preceding fraction; this fraction was not analyzed further. Subsequent cochromatography (HPLC and/or TLC) with reference standards, and analysis by capillary liquid chromatograpy/mass spectrometry led to the identification of above metabolites. The structure and names are listed in the following table.

Raw urine from the goat treated with the 14C-pyrimidinyl (#2) was first incubated with various enyzmes, then eluted from a resin column into 3 fractions. The 14C-activity was present in all three fractions. HPLC analysis of fraction 3 showed parent only, while fraction 1 gave parent plus metabolite M1. Fraction 2 contained <20% of the urinary 14C, and HPLC analysis showed numerous peaks; this fraction was not analyzed further. Subsequent cochromatography (HPLC and/or TLC) with reference standards, and analysis by capillary liquid chromatography/mass spectrometry led to the tentative identification of metabolite M1 as a polar conjugate of 5-hydroxy pyrimidine amine (See table for structure). However, efforts to discover the polar moiety by enyzmatic hydrolyses with β-glucuronidase, α-glutamyltranspeptidase, and sulfatase, followed by HPLC analysis, were unsuccessful.

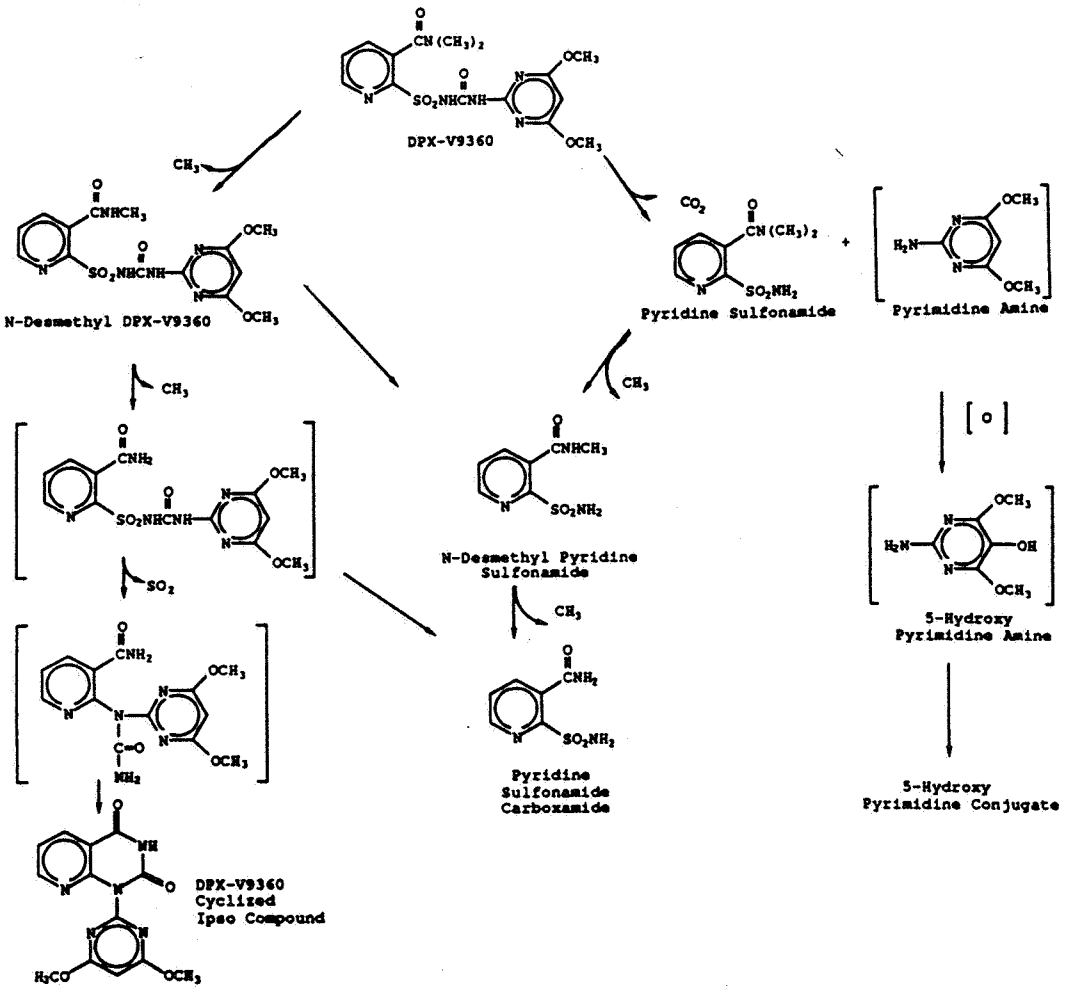
A bile sample from goat #1 (pyridinyl-labelled) was apparently analyzed raw without a cleanup. The major residue was the parent (85%); minor residues (15%) were not defined. No sample was presented for goat #2. Likewise, a fecal sample from goat #1 was extracted and subjected to HPLC analysis. The major residue was the parent (>90%); minor extractable, or unextractable residues, were not defined. No sample was presented for goat #2.

A liver sample from goat #2 (pyrimidinyl-labelled) was extracted and analyzed by HPLC. The extracted liver was vacuum dried and combusted to determine the remaining 14C-activity. According to the submitted HPLC chart >50% was identified as parent. The remaining 14C-activity (<50%) was divided amongst numerous peaks, none of which appeared to be >10% of the total 14C-activity in the liver. No liver sample was presented for goat #1.

The total 14C-activities in milk, kidney, fat, or muscle were not characterized.

The proposed metabolic pathway for DPX-V9360 in the goat showed primarily three mechanisms: 1) hydrolysis of the sulfonylurea bridge to yield pyridine sulfonamide and pyrimidine amine (both of which undergo additional metabolism); 2) N-demethylation and subsequent loss of sulfur dioxide leading to the cyclized compound N2; and 3) oxidation and conjugation at the 5-position of the pyrimidine ring.

Proposed Metabolic Pathway for DPX-V9360 in the Goat:



While the major pathway in the rat is also hydrolysis of the sulfonylurea bridge, some of the metabolites observed in the goat were not identified in the rat, i.e., the cyclized compound N3 and M1. In the rat, several metabolites, MU "A", MF "A", and MF #1 were found in the urine and feces from rat dosed with pyridinyl 14C-labelled DPX-V9360. Metabolites MU "A" and MF #1 were tentatively assigned as pyridine acid sulfonamide. This free acid was not identified in the goat, but potential precurors, i.e., metabolites N3, N4, and N5, were isolated and identified. Metabolite N3 was also isolated from the rat urine. Metabolite MF "A" was not identified. With the pyrimidinyl 14C-labelled DPX-V9360, 5-OH pyrimidine amine was isolated in the rat, while a conjugate of this compound, M1, was isolated in the goat. Therefore the metabolic pathways are very similar. Perhaps, the small differences in compounds identified can adequately be explained by slight differences in the isolation and purification procedures for each study.

In this submission, PP#9F3763, the petitioner has not provide any poultry metabolism studies.

According to the petitioner this is justified because at the proposed treatment rate the harvested grain, which would be the r.a.c. used for feeding poultry, contains no detectable residues of DPX-V9360 (<0.05 ppm), or any significant metabolites as evidenced by the plant metabolism study.

According to a recent decision (See memo of 7/25/89, R. Schmitt) DEB could require a poultry metabolism study for DPX-V9360. DEB has requested additional field residue data for DPX-V3960 and metabolite pyridine sulfonamide. Dependent upon these results, e.g., real residues of pyridine sulfonamide (>0.05 ppm) are found in harvested corn grain, a poultry metabolism study may be needed.

171-4: Analytical Enforcement Method

Analytical methodologies are submitted for nicosulfuron (DPX-V9360) in/on corn forage, fodder, silage, and grain. The method is for parent only; methods were not submitted for its metabolites.

Method: "Analytical Method for the Quantitation of DPX-V9360 in Corn (Forage, Fodder, Silage, and Grain)", E. I. du Pont de Nemours & Co., Inc., January 23, 1989. (MRID#410826-32).

The method utilizes a reverse phase HPLC assay and quantification of the a.i., DPX-V9360, with UV detection at 254 nm. The petitioner describes two methods of analysis: the first involves the use of two HPLC systems, one for initial cleanup of the sample extract, and the second for the analytical determination. Where only several samples require analysis, i.e., for enforcement purposes, one HPLC can be used. The sample is first injected for cleanup, then the sample loop, column, and eluent are changed to allow analysis.

The analyte is extracted from the sample with a 20% MeOH:80% pH 8 aqueous buffer as the extraction solution prepared as follows: Mix 160 ml of 1M K_2HPO_4 with 1440 ml of water; adjust the pH of this solution to pH 8.0 by the addition of concentrated H_3PO_4 (1-1.5 ml). Add 400 ml of MeOH and mix. Final pH should be about 8.4.

For the extract process, forage, fodder, or silage samples are chopped frozen in the presence of dry ice. Corn grain is removed from the ears and ground frozen in a grinding mill. A 10 g sample is extracted by homogenization with 100 ml of the above extraction solution. The homogenized sample is centrifuged, and the supernatant is acidified with concentrated H_3PO_4 until pH 2.5 to 3.5. After setting for 15 minutes to allow for formation of precipitates, the acidified mixture is centrifuged and the supernatant is decanted for injection on the HPLC.

The analysis can be interrupted before the acidification step, and the sample can be stored for at least 2 days at 4°C without a loss of any DPX-V9360 residues. If the analysis must be delayed for more than 2 to 4 hours after the acidification step, then the sample should be refrigerated because DPX-V9360 is thermally unstable under acidic conditions. However, refrigeration is effective in the hinderance of this degradation. Samples should be returned to room temperature prior to HPLC injection.

The stability of DPX-V9360 in the extraction procedure was validated by adding 14C-labelled DPX-V9360 (either in the pyridine or the pyrimidine ring) to the acetone: ammonium carbonate solution, and processing according to the directions. HPLC analysis showed that no significant degradation occurred.

The initial HPLC sample cleanup is performed on a Zorbax® Phenyl column with an aqueous eluent of 38% MeOH buffered at pH 3.5 (KH_2PO_4/H_3PO_4). A DPX-V9360 standard is injected to determine the retention time under the HPLC conditions. Then after injection of the plant extract (5 ml sample) the eluent is collected, ca. 2 mintues before the retention time and continued until ca. 3 minutes after, in a 10 ml volumetric flask (ca 6.5 ml collected). One drop of concentrated H_3PO_4 is added to this collected fraction which is then diluted to volume. A 2.0 ml sample is injected for the analytical determination on a Zorbax®R_X™. An aqueous eluent of 18% MeOH buffered at pH 6.20 (KH_2PO_4/H_3PO_4) is used for the analysis. DPX-V9360 standards in the sample extraction solution require acidification with concentrated H_3PO_4 to pH 2.5 to 3.5 before chromatography on the analytical HPLC. Samples and standards are best kept refrigerated until analyzed. These should be returned to room temperature prior to analysis.

If a significant interference is apparent, the pH of eluent for the analytical run (18% MeOH:pH 6.20) may be adjusted to selectively move the DPX-V9360 peak relative to the interference. A pH drop of 0.25 units will increase the DPX-V9360 retention time by approximately 2 minutes. Also confirmation of DPX-V9360 in the presence of other pesticides can be achieved using a Zorbax® Phenyl column in place of the analytical Zorbax®R_X™ but still with the 18% MeOH:pH 6.20 buffered eluent.

Recovery data are presented for DPX-V9360 at levels of 0.05, 0.10, 0.25, and 0.50 ppm in forage, silage, fodder, and grain. The percentages recovery ranged from 80 to 101%. The extraction efficiency and storage stability were checked using forage samples treated with either [pyridine-2-14C]DPX-V9360 (14-day PHI, 1X rate; 30-day PHI, 2X rate) or [pyrimidine-2-14C]DPX-V9360 (14-day PHI, 1X rate; 30-day PHI, 2X rate). The 14C-activity extracted ranged from 89 to 94%. Data were not provided for silage, fodder, or grain. Storage stability data (MRID#410826-28) are also provided for corn forage samples treated with either of the labelled materials and stored under freezer conditions for 7 months at -20°C. Liquid scintillation counting and HPLC analyses showed essentially little degradation of DPX-V9360 residues under these conditions. The storage stability data is adequate for parent DPX-V9360 residues in corn grain, forage, and fodder.

The herbicide DPX-V9360 has been tested through the FDA Multi-Residue Protocols I, II, III, and IV. Since DPX-V9360 is thermally labile, the GLC protocols I, II, and III were not suitable. Only Protocol IV was run with DPX-V9360. This method was not applicable because the herbicide did not give a detectable response on the required HPLC/fluorescence detection system. This data has been forwarded to FDA for review (See memo of 11/8/89, J. Stokes).

If interferences from other pesticides occur during the analysis of DPX-V9360, the petitioner stated that the pH of the HPLC eluent may be adjusted slighty to selectively move the DPX-V9360 peak relative to the interference. No sample charts or other data are provide to support this method. Additional data, i.e., sample HPLC charts in which this statement is adequately supported, should be submitted to DEB for review. These "interference peaks" should be an adequate representation of current pesticides used on corn, and to include examples of other sulfonylureas shown to behave similarily.

A PMV has been performed by ACS, ACB, BEAD (See memo of 2/23/90, E. Hayes) for corn forage, grain, and fodder. The method gave good recoveries of 0.1 and 0.2 ppm DPX-V9360 spiked samples of grain (83 to 95%), forage (84 to 90%), and fodder (75 to 107%). Initially, the EPA lab had difficultly with the local fodder sample, but after the company supplied a fodder sample, the lab was able to achieve the analysis according to the submitted methodology. The lab found 1) the method to be time consuming, requiring the use of two LC units, 2) the cleanup column can become plugged if the extract is not centrifuged at 20,000 rpm, 3) if the fodder is dry, additional solvent may be required, 4) the continuous backflushing on the cleanup column will shorten life quickly, 5) the 2.0 ml injections on the analytical column will likewise drastically shorten the life span of this column, 6) it is critical to monitor and maintain the pH of all mobile phases, as the peaks can shift drastically with a small pH change, and 7) the split mode required two day to run six samples.

Thus, according to the above report and the included comments from the EPA lab the method is workable for corn forage and grain, but as submitted, could present problems on corn fodder even for an experienced analyst. The petitioner should submit the characteristics of the corn fodder supplied to the Agency laboratory for the PMV, e.g., maturity at harvest, moisture content, with or without ears, etc. After reviewing this information the proposed enforcement method may require rewriting or modification for this commodity. The petitioner should also specify in the clarification/rewrite of the method that the pH levels of all mobile phases must be closely monitored and maintained accurately according to instructions. The petitioner must properly define the Zorbax™R_X column. Is it a C8 or C18 bonded phase?

The petitioner must submit validation data, sample charts, etc., to support the methodology used to analyze the corn forage, fodder, and grain for the metabolite pyridine sulfonamide, including storage stability data.

The need for additional analytical methodology for DPX-V9360 and/or metabolite pyridine sulfonamide in regards to livestock meat and meat by-products, milk, and eggs, will be determined after the requested field residue data have been reviewed and the need for any feeding studies have been determined. If metabolite pyridine sulfonamide is added to the tolerance expression, then this residue must be evaluated with the FDA multiresidue protocols.

171-4: Magnitude of the Residue

Crop Field Trials:

Studies from 14 representatives test sites (13 states which represented 74% of total US corn production, Ag Stat. 1987) were conducted with the herbicide DPX-V9360. DPX-V3960 was applied at the maximum label rate of 1.0 oz a.i./A (1X) and at a 2X rate of 2.0 oz a.i./A, in 13 to 69 gallons of water. Treatment was made at the 5- to 10-leaf stage on 9 field corn varieties. Treated and control samples of forage, silage, fodder, and grain were retrieved at PHI's ranging from 14 to 49 days, 45 to 82 days, 72 to 128 days, and 72 to 128 days, respectively. All samples were stored frozen until analysis and were analyzed according to the proposed enforcement methodology for parent only. Only ground application data has been submitted. The label restricts the application to ground only.

Sampling Summary

Site	PHI (days) Forage	Silage	Fodder	Grain
Cutler, IN	21,32,46	74	--	--
Darien, WI	15,30,45	65	128	128
Davis, CA	15,30,44	79	119	119
Fort Valley, GA	15,28,42	68	92	92
Hollandale, MN	15,30,45	64	99	99
Humboldt, IA	15,30,43	64	122	122
Lexington, TN	15,30,44	45	93	93
New Holland, OH	14,29,46	77	120	120
Oakland, NE	15,30,45	80	116	116
Rives Junction, MI	15,30,45	62	115	115
Rochelle, IL	15,30,45	79	125	125
Vicksburg, MS	14,28,47	59	118	118
Walton, KS	16,30,45	58	72	72
Whiteland, IN	15,29,49	82	121	121

Residues of DPX-V9360 on Forage, Silage, Fodder, and Grain

Sample	Rate (oz a.i./A)[a]	PHI(days)	Residues (ppm)[b]
forage	1.0	14-21	<0.05 - 0.23[c]
		28-32	<0.05
		42-49	<0.05
forage	2.0	14-21	<0.05 - 0.70[d]
		28-32	<0.05 - 0.06[e]
		42-49	<0.05
silage	1.0	45-85	<0.05
silage	2.0	45-85	<0.05
fodder	1.0	72-128	<0.05
fodder	2.0	72-128	<0.05
grain	1.0	72-128	<0.05
grain	2.0	72-128	<0.05

[a] 1.0 oz a.i./A and 2.0 oz a.i./A represent 1X and 2X, respectively.

[b] Analytical methodology measures parent, DPX-V9360, only.

[c] Of 10 samples, 3 gave residues $\geq$ limit of detection (0.05 ppm): 0.05, 0.07, and 0.23.

[d] Of 9 samples, 4 samples gave residues $\geq$ limit of detection: 0.05, 0.14, 0.28, 0.70.

[e] Of 14 samples, only one gave residues $\geq$ limit of detection: 0.06.

No measurable residues (<0.05 ppm) were found in forage samples at the proposed 30-day PHI at the maximum proposed 1.0 oz a.i./A. application rate. Also only in one case (2X application rate) were residues detected, 0.06 ppm (day 29), and this was almost at the limit of detection (0.05 ppm). No detectable residues (<0.05 ppm) were found in any samples of silage, fodder, or grain at either the 1X or 2X application rates. Fortified control samples were spiked at 0.05 or 0.10 ppm DPX-V9360, then extracted and analyzed according to the proposed HPLC enforcement analytical methodology.

A decline curve for both the 1X and 2X application rates, 1.0 and 2.0 oz a.i./A, respectively, showed a half life of 2 days under field conditions for the parent DPX-V9360. Data was not presented for the metabolite pyridine sulfonamide.

Based upon the residue data, the submitted decline curve, and the corn plant metabolism data, it appears that DPX-V9360 rapidly degrades in corn, and that concentration of the parent decreases below the 0.05 ppm detection limit within the proposed 30-day PHI. This would adequately support the proposed 0.10 ppm tolerance on corn forage, silage, fodder, and grain when applied postemergence to corn at 1.0 oz a.i./A. The submitted data also supports a 60-day PHI for corn silage, and a 90-day PHI for corn fodder and grain for residues of the parent DPX-V3960.

The analytical methodology limit of detection is 0.05 ppm and will only define the parent. Based upon the total 14C-radioactivity <0.07 ppm could be present in the stalk. Metabolite pyridine sulfonamide could be a major portion of this activity. The petitioner mentioned rotational crop guidelines in the proposed label, and divided the US by state and soil pH into three groups, A, B, and C. Most of the data has been submitted from Group A, with only one state in Group B, and one in Group C.

Therefore, since 1) no feeding studies and no requested tolerances on livestock meat, meat byproducts, milk, or eggs, are available, and to support the assumption that <0.05 ppm DPX-V9360 residues are on all corn commodities, and 2) the soil pH could affect the persistence of DPX-V9360 and the formation of any levels of metabolite pyridine sulfonamide, DEB will require the submission of additional residue data.

The petitioner must submit additional residue data from states in Groups B and C. According to the label ACCENT™ should not be applied to soil with a pH above 7.5; data submitted in which soil above pH 7.5 will not be acceptable. The petitioner must analyze for the parent DPX-V9360 and metabolite pyridine sulfonamide. In addition, the petitioner must reanalyze previously submitted samples from six different US locations (which were analyzed for DPX-V9360 residues) for the metabolite pyridine sulfonamide. Three samples of forage, three samples of fodder, and three samples of grain from each location must be submitted.

Based upon the already submitted residue data the proposed tolerances on corn forage, silage, fodder, and grain could be changed from 0.1 ppm to 0.05 ppm. If real residues of pyridine sulfonamide are found in these corn commodities, then the appropiate tolerances must also be proposed in a revised Section F.

Processed Food/Feed:

Dry mill processing : (MRID#410826-30, DuPont Study #AMR 1191-88)

Residue data are submitted from corn plants treated with DPX-V9360 at a rate of 8.0 oz a.i./A (8X the proposed rate). The harvested

corn grain (127 day PHI) was processed into fractions, i.e., corn meal and crude corn oil, by a laboratory simulation of commercial corn dry milling methods. The analyses were perform using the proposed HPLC enforcement analytical methodology. Control samples of the corn fractions were spiked for use in method validation studies. (Note: store-bought oil had to be used for spiked samples because the volume of oil generated in the lab simulation was too small.) Recovery data for fortified corn meal, 0.05 to 0.50 ppm DPX-V9360, ranged from 80 to 100%. Laboratory generated oil fortified at 0.05 to 0.50 ppm DPX-V9360 gave recoveries ranging from 53 to 97%, and for store oil fortified at the same levels from 55 to 113%. No measurable residues (<0.05 ppm) of DPX-V9360 were found in the processed commodities of corn meal and corn oil (25X potential concentration factor) harvested from a crop treated at an exaggerated 8X rate. No measurements were taken for levels of metabolite pyridine sulfonamide. The petitioner must reanalyze the meal and oil samples for residues of metabolite pyridine sulfonamide. Storage stability data must be included. The petitioner must also submit the pH of the soil used in the 8X application rate.

DEB will withhold comment on the need for feed/food additive tolerances for DPX-V3960, and possibly metabolite pyridine sulfonamide, on processed corn commodities from the dry milling process until the requested residue data have been reviewed. In addition, DEB must reserve the right to request a wet milling process, and any subsequent tolerances, for the proposed DXP-V9360 postemergence use until the above requested residue data have been reviewed.

Milk, Meat, Polutry, and Eggs:

No ruminant feeding studies are submitted. The petitioner stated that since no detectable DPX-V9360 residues (<0.05 ppm) were found in forage (30-day PHI), silage, fodder, and corn grain at the proposed maximum rate of 1.0 oz a.i./A, then measurable secondary residue would not be detectable in milk, meat, or meat byproducts (including liver and kidney) for the proposed postemergence use.

No poultry feeding studies are submitted. Again, the petitoner stated that since no detectable DPX-V9360 residues (<0.05 ppm) were found in forage (30-day PHI), silage, fodder, and corn grain at the proposed maximum rate of 1.0 oz a.i./A, then measurable secondary residue would not be detectable in poultry meat, or meat byproducts (including liver and kidney), or eggs for the proposed postemergence use.

Residues are reportedly not detected (<0.05 ppm) for DPX-V9360 even at exaggerated application rates in grain (2X and 8X) and in forage, silage, or fodder (2X; not reported for 8X; 30-day PHI). The goat metabolism study was conducted at a feeding level of 60 ppm/day for three days (1200X feeding level with reference to the 0.05 ppm detection limit).

As stated in this memo in "Nature of the Residue (animals)", DEB will not require a poultry metabolism study at this time. Likewise, DEB will not require a poultry or ruminant feeding study at this time. DEB has required the submission of additional residue data for DPX-V9360 and metabolite pyridine sulfonamide in raw agricultral corn commodities. After review of the requested data, DEB will determine the need for a poultry metabolism study and/or a poultry and/or ruminant feeding study.

We reserve our conclusion on secondary residues in meat, milk, poultry, and eggs, until we have received and reviewed the residue data requested above for the parent and metabolite pyridine sulfonamide.

International Residue Limit Status: Codex

No Codex tolerances, or Canadian or Mexican Limits are established for a food use for DXP-V9360 (nicosulfuron). Therefore, there are no problems of incompatability.

Attachments: 1) Confidential Appendix
2) International Residue Limit Status (Codex)

cc with Confidential Attachment and Codex: J. Stokes (DEB), PP#9F3763, C. Furlow (PIB/FOD), Nicosulfuron S. F.

cc without Confidential Attachment/with Codex: R. F.;
Circulation (7)
RDI: PErrico:4/17/90:RLoranger:4/20/90
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DATA REQUIREMENTS FOR Nicosulfuron (DPX-V9360) TECHNICAL PRODUCTS[1/] (EPA REG. NO. 352-LGL; E. I. du Pont de Nemours & Company, Inc.)

Table A

Data Requirement	Test Substance[2/]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Time Frame For Submission
158.240 Residue Chemistry					
171-2. Chemical Identity[3/]	TGAI	Partially	MRID#409545-01	Yes	
171-3. Directions for Use	TEP	Yes		No	
171-4. Nature of the Residue (Metabolism) -Plants	PAIRA	Partially	MRID#410826-26	Yes[4/]	
-Livestock	PAIRA	Partially	MRID#410826-27	Yes[5/]	
171-4. Residue Analytical Methods					
-Plant and Animal Residues	TGAI and metabolites	Partially	MRID#410826-32	Yes[6/,7/]	
171-4. Magnitude of the Residue	TEP				
-Crop Field Trials		Partially	MRID#410826-29	Yes[8/]	
-Storage Stability Data		Partially	MRID#410826-28	Yes[9/]	

DATA REQUIREMENTS FOR Nicosulfuron (DPX-V9360) TECHNICAL PRODUCTS[1/] (EPA REG. NO. 352-LGL; E. I. du Pont de Nemours & Company, Inc.)

Table A (continued)

Data Requirement	Test Substance[2/]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?	Time Frame For Submission
158.240 Residue Chemistry					
171-4. Magnitude of the Residue	TEP				
-Processed food/feed		Partially	MRID#410826-30	Yes[10/]	
-Storage Stability Data		Partially	MRID#410826-30	Yes[11/]	
-Meat/milk/poultry/eggs		Partially	MRID#410826-32	Yes[12/, 13/, 14/]	
-Storage Stability Data		Partially	MRID#410826-32	Yes[15/]	

1/ The chemical name for DPX-V9360 (ACCENT™) is 3-pyrimidinecarboxamide, 2-((((4,6dimethoxypyrimidin-2-yl) aminocarbonyl)aminosulfonyl))-N,N-dimethyl. The common name is nicosulfuron (ISO approved, ANSI proposed)

2/ Composition: TGAI = technical grade active ingredient; PAIRA = pure active ingredient radiolabeled; TEP = typical end use product.

3/ The same chemical identity as required under 158.150, 158.160, 158.162, 158.167, 158.170, 158.175, 158.180, and 158.190 are required, with emphasis on impurities that could constitute a residue problem. (See Table A, Product Chemistry Requirements, this memo).

4/ The pH of the soil used in the metabolism study must be submitted. The primary residue of regulatory concern is the parent DPX-V9360. Additional residue data must be reviewed before final determination if metabolite pyridine sulfonamide must be included.

5/ A poultry metabolism study may be needed. Additional residue data must be reviewed before final determination.

6/ Additional residue data has been requested for metabolite pyridine sulfonamide in/on corn commodities. Storage stability data for metabolite must be submitted. Dependent upon the results analytical methodology may be needed.

7/ Additional data must be submitted to support the proposed procedure to analyze for DPX-V9360 residues in the presence of other pesticides which could cause interference in the analysis.

8/ Additional residue data must be submitted for metabolite pyridine sulfonamide.

9/ Storage stability data for metabolite pyridine sulfonamide in support of the proposed use must be submitted.

10/ The processed commodities of corn oil and meal must analyzed for metabolite pyridine sulfonamide.

11/ Storage stability data must be submitted for metabolite pyridine sulfonamide.

12/ Based upon the proposed use, no detectable DPX-V93260 residues (<0.05 ppm) should be in milk, meat, fat, or byproducts (including liver and kidney) of cattle, horses, swine, sheep, or goats. Analytical methodology should not be needed for the proposed postemergence use on field corn. Additional residue data must be reviewed before final determination.

13/ No decision will be made in regards to poultry meat, fat, meat byproducts (including liver and kidney) and subsequent analytical methodology until the additional residue data has been reviewed.

14/ Dependent upon the requested residue data, a poultry feeding study may be needed.

15/ Storage stability data will be needed if the feeding study is required.

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL nicosulfuron, DPX-V9360

CODEX NO. _____

CODEX STATUS:

|X| No Codex Proposal Step 6 or above

Residue(if Step 8): _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 9F3763

RCB Reviewer J. Stokes

Residue: nicosulfuron, DPX-V9360

Crop(s)	Limit (mg/kg)
corn forage	0.1
corn silage	0.1
corn fodder	0.1
corn grain	0.1

CANADIAN LIMITS:

|X| No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

|X| No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES: